

Listing of Claims:

1-9: (Cancelled)

10. (Original) A method of determining the effect of a drug lead on the activity of a drug-metabolizing enzyme comprising:

(a) providing a drug lead that shifts the thermal unfolding curve of a receptor regulating cytochrome P450 expression; and

(b) screening the drug lead for its ability to further shift the thermal unfolding curve of the receptor in the presence of one or more co-regulators; wherein a further shift in the thermal unfolding curve of the receptor in the presence of the drug lead and a co-regulator of said one or more co-regulators indicates whether the drug lead increases the activity of a drug-metabolizing enzyme.

11. (Original) The method of claim 10, wherein providing a drug lead that shifts the thermal unfolding curve of the receptor comprises screening one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the receptor.

12. (Original) The method of claim 11, wherein said screening of one or more of a multiplicity of different molecules comprises:

(a) contacting said receptor-regulating cytochrome P450 and one or more molecules in each of a multiplicity of containers;

(b) heating said receptor in each of said multiplicity of containers to cause said receptor to unfold;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said receptor;

(d) generating a thermal unfolding curve for said receptor for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to:

(i) each of the other thermal unfolding curves; and/or

(ii) the thermal unfolding curve for said target molecule in the absence of any of said multiplicity of molecules; and

(f) determining whether any of said multiplicity of molecules shifts the thermal unfolding curve of said receptor.

13. (Presently Amended) The method of claim 10 ~~or claim 12~~, wherein said screening step further comprises:

(a) contacting said drug lead and said receptor regulating cytochrome P450 expression with one or more of said co-regulators in each of a multiplicity of containers;

(b) heating said receptor in each of said multiplicity of containers to cause said receptor to unfold;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said receptor;

(d) generating a thermal unfolding curve for said receptor for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to:

(i) each of the other thermal unfolding curves; and/or

(ii) the thermal unfolding curve for said receptor in the absence of (1) said drug lead and/or (2) said co-regulators; and

(f) determining whether said drug lead further shifts the thermal unfolding curve of said receptor.

14. (Original) The method of claim 10 wherein the one or more co-regulators includes a co-activator and/or co-repressor.

15. (Original) The method according to claim 10, wherein the molecule further modifies the stability of the receptor in the presence of a co-activator, thereby identifying the ligand as an agonist of the receptor when in the presence of the co-activator.

16. (Original) The method according to claim 15, wherein the agonist is a partial agonist.

17. (Original) The method according to claim 10, wherein the molecule further modifies the stability of the receptor in the presence of a co-repressor, thereby identifying the ligand as a non-agonist of the receptor when in the presence of the co-activator.

18. (Original) The method according to claim 17, wherein the non-agonist is a partial agonist.

19-21. (Cancelled)

22. (Original) A method of identifying an agonist of xenobiotic metabolism comprising screening a molecule for its ability to shift the thermal unfolding curve of a receptor regulating cytochrome P450 expression and to further shift the thermal unfolding curve of said receptor when in the presence of one or more co-activators; wherein a molecule that shifts the thermal unfolding curve of said receptor and further shifts the thermal unfolding curve of said receptor when in the presence of a co-activator is identified as an agonist of xenobiotic metabolism.

23. (Original) The method of claim 22, wherein said screening step further comprises:

(a) contacting said molecule and said receptor regulating cytochrome P450 expression with one or more of said co-activators in each of a multiplicity of containers;

(b) heating said receptor in each of said multiplicity of containers to cause said receptor to unfold;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said receptor;

(d) generating a thermal unfolding curve for said receptor for each of said containers ;

(e) comparing each of said thermal unfolding curves in step (d) to:

(i) each of the other thermal unfolding curves; and/or

(ii) the thermal unfolding curve for said receptor in the absence of (1) said molecule and/or (2) said co-activators; and

(f) determining whether said molecule further modifies the stability of said receptor, wherein a further modification in stability is indicated by a further change in said unfolding curve.

24. (Original) A method according to claim 22, wherein the agonist is a partial agonist.

25-26. (Cancelled)

27. (Original) A method of identifying a non-agonist of xenobiotic metabolism comprising screening a molecule for its ability to shift the thermal unfolding curve of a receptor regulating cytochrome P450 expression; wherein a molecule that does not shift the thermal unfolding curve of said receptor is identified as a non-agonist of xenobiotic metabolism.

28. (Original) The method of claim 27, wherein said screening step comprises:

(a) contacting said receptor regulating cytochrome P450 and one or more molecules in each of a multiplicity of containers;

(b) heating said receptor in each of said multiplicity of containers to cause said receptor to unfold;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said receptor;

(d) generating a thermal unfolding curve for said receptor for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to:

(i) each of the other thermal unfolding curves; and/or

(ii) the thermal unfolding curve for said target molecule in the absence of any of said multiplicity of molecules; and

(f) determining whether said molecule modifies the thermal unfolding curve of said receptor.

29-60. (Cancelled)

61. (Currently Amended) A method according to ~~any of claims 1-60~~ claim 10, wherein the co-regulator is a co-activator and/or a co-repressor.

62. (Currently Amended) A method according to ~~any of claims 1-60~~ claim 10, wherein an agonist for a co-regulator dependent receptor is a strong inducer.

63. (Original) A method according to claim 62, wherein the strong inducer is 11- α -hydroxyprogesterone.

64. (Currently Amended) A method according to ~~any of claims 1-60~~ claim 10, wherein the strong inducer has a binding affinity of less than about 5 μ M and a statistical probability of agonist state of about 0.8 to about 1.0.

65. (Currently Amended) A method according to ~~any of claims 1-60~~ claim 10, wherein a partial agonist of a co-regulator dependent receptor is a weak inducer.

66. (Original) A method according to claim 65, wherein the weak inducer has a binding affinity of less than about 5 μ M and a statistical probability of agonist state of about 0.4 to about 0.8.

67. (Original) a method according to claim 65, wherein the weak inducer has a binding affinity of at least about 5 μ M and a statistical probability of agonist state of about 0.4 to about 1.0.

68. (Currently Amended) A method according to ~~any of claims 1-60~~ claim 10, wherein an antagonist of a co-regulator dependent receptor is a non-inducer.

69. (Original) A method according to claim 68, wherein the non-inducer has a binding affinity of less than about 5 μ M and a statistical probability of agonist state of less than about 0.4.

70. (Original) A method according to claim 65, wherein the non-inducer has a binding affinity of at least about 5 μ M and a statistical probability of agonist state of less than about 0.4.